Image 147

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 00-1229)

PATENT

In re Application of: Paszty et al.

Serial No.: 09/928,175 **Before the Examiner: J. Seharaseyon**

Filed: August 10, 2001 **Group Art Unit: 1647**

For: Leucine-Rich Repeat-Containing G-Protein Coupled Receptor-8 Molecules and Uses Thereof)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

TRANSMITTAL LETTER

1. We are transmitting herewith the attached papers for the above-described patent application: Response to Restriction Requirement and return postcard.

2. GENERAL AUTHORIZATION TO CHARGE OR CREDIT FEES: Please charge any additional fees or credit any overpayment to Deposit Account No. 13-2490.

3. CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8: The undersigned hereby certifies that this Transmittal Letter and the papers, as described in paragraph 1, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington D.C. 20231, on November 6, 2003.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: November 6, 2003

By: Donald L. Zuhn, Ph.D.
Reg. No. 48,710

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
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P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

RESPONSE TO RESTRICTION REQUIREMENT MAILED OCTOBER 6, 2003

Responsive to the Restriction Requirement mailed October 6, 2003, Applicants elect to prosecute claims 1-12 and 42-45, designated as the invention of Group I by the Action, which the Action states are drawn to a nucleic acid molecule encoding a polypeptide, a vector, and a host cell. The Action also states that the claims of Group I and II are drawn to multiple sequences (SEQ ID NO: 1-23) that constitute independent and distinct inventions because the sequences lack common structural or functional properties. Applicants, therefore, further elect to prosecute the nucleotide sequence of SEQ ID NO: 1, with traverse. The basis for Applicants' traversal of the requirement is as follows.

Applicants respectfully submit that there will be no undue hardship on the Office in performing a search with respect to the nucleotide sequences of SEQ ID NOs: 1, 4, 6, 9, 11, 14, and 16, because a search with respect to any one sequence would necessarily uncover all art that is pertinent to each of the other sequences. Applicants note that the instant application teaches that the LGR8-A coding sequence consists of 18 exons that encode a large N-terminal leucine-rich repeat-containing extracellular domain, seven predicted transmembrane domains, and a cytoplasmic C-terminal region (page 3, lines 6-8). Applicants also note that the instant application teaches that the

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Donald L. Zuhn

present invention relates, in part, to four distinct human LGR8 alternative splicing variants (page 3, lines 5-6). Specifically, the instant application teaches that (1) human LGR8-B differs from human LGR8-A only in that human LGR8-B lacks one of the exons encoding the N-terminal extracellular domain of human LGR8-A (page 3, lines 8-10); (2) human LGR8-C differs from human LGR8-A only in that human LGR8-C lacks three exons encoding the N-terminal extracellular domain of human LGR8-A (page 3, lines 11-13); and (3) human LGR8-D differs from human LGR8-A only in that human LGR8-D lacks exons encoding a portion of the N-terminal extracellular domain and the transmembrane domains and cytoplasmic C-terminal region of human LGR8-A (page 3, lines 13-16), and that LGR8-D is truncated by virtue of an insertion of an additional exon containing a stop codon (page 3, lines 17-20).

The nucleotide sequences set forth in SEQ ID NO: 1 (human LGR8-A coding sequence) and SEQ ID NO: 6 (human LGR8-B coding sequence) encode polypeptides of 754 and 730 amino acids, respectively. Exhibit A illustrates that human LGR8-A and human LGR8-B differ *only* in that human LGR8-B lacks amino acid residues 287-311 of human LGR8-A, and that the encoded proteins are otherwise 100% identical. The nucleotide sequences set forth in SEQ ID NO: 1 and SEQ ID NO: 11 (human LGR8-C coding sequence) encode polypeptides of 754 and 682 amino acids, respectively. Exhibit B illustrates that human LGR8-A and human LGR8-C differ *only* in that human LGR8-C lacks amino acid residues 191-214, 287-311, and 335-358 of human LGR8-A, and that the encoded proteins are otherwise 100% identical. The nucleotide sequences set forth in SEQ ID NO: 1 and SEQ ID NO: 16 (human LGR8-D coding sequence) encode polypeptides of 754 and 366 amino acids, respectively. Exhibit C illustrates that human LGR8-A and human LGR8-D differ *only* in that human LGR8-D lacks amino acid residues 287-311 of human LGR8-A and possesses an additional exon encoding eight amino acids and containing a stop codon. These proteins are otherwise 100% identical. The ClustalW sequence alignments shown in Exhibits A-C were performed using the application MacVector 7.1.1 (Accelrys, Cambridge, UK; http://www.accelrys.com) at the default settings.

Applicants also traverse the restriction of the nucleotide sequences set forth in SEQ ID NOs: 4, 9, and 14. Applicants note that the instant application teaches that the present invention relates, in part, to the N-terminal extracellular domains of human LGR8-A, LGR8-B, and LGR8-C, which are

likely to function as antagonists of the LGR8 signaling pathway (page 3, lines 21-22). Specifically, the instant application teaches that (1) the nucleotide sequence of SEQ ID NO: 4 encodes the N-terminal domain of human LGR8-A, absent the signal peptide (page 12, lines 5-6); (2) the nucleotide sequence of SEQ ID NO: 9 encodes the N-terminal domain of human LGR8-B, absent the signal peptide (page 12, lines 11-12); and (3) the nucleotide sequence of SEQ ID NO: 14 encodes the N-terminal domain of human LGR8-C, absent the signal peptide (page 12, lines 17-18).

Exhibit D illustrates that the polypeptides encoded by nucleotide sequence of SEQ ID NO: 1 (human LGR8-A) and SEQ ID NO: 4 (N-terminal extracellular domain of human LGR8-A) differ *only* in that the polypeptide encoded by SEQ ID NO: 4 is truncated at its N-terminal and C-terminal ends, and that the encoded proteins are otherwise 100% identical. Exhibit E illustrates that the polypeptides encoded by nucleotide sequence of SEQ ID NO: 6 (human LGR8-B) and SEQ ID NO: 9 (N-terminal extracellular domain of human LGR8-B) differ *only* in that the polypeptide encoded by SEQ ID NO: 9 is truncated at its N-terminal and C-terminal ends, and that the encoded proteins are otherwise 100% identical. Exhibit F illustrates that the polypeptides encoded by nucleotide sequence of SEQ ID NO: 11 (human LGR8-C) and SEQ ID NO: 14 (N-terminal extracellular domain of human LGR8-C) differ *only* in that the polypeptide encoded by SEQ ID NO: 14 is truncated at its N-terminal and C-terminal ends, and that the encoded proteins are otherwise 100% identical. Exhibits D-F illustrate, therefore, that the polypeptides encoded by the nucleotide sequences set forth in SEQ ID NOs: 4, 9, and 14 are merely fragments of the polypeptides encoded by the nucleotide sequences set forth in SEQ ID NOs: 1, 6, and 11, respectively. The ClustalW sequence alignments shown in Exhibits D-F were performed using the application MacVector 7.1.1 (Accelrys, Cambridge, UK; http://www.accelrys.com) at the default settings.

Applicants respectfully submit that because the nucleotide sequences of SEQ ID NOs: 1, 4, 6, 9, 11, 14, and 16 share substantial sequence identity, and therefore, share, rather than lack, common structural properties, there will be no undue hardship on the Office in performing a search with respect to the nucleotide sequences of SEQ ID NOs: 1, 4, 6, 9, 11, 14, and 16, as a search of any one sequence would necessarily uncover all art that is pertinent to each of the other sequences.

Applicants do not believe that any additional fee is required. However, the Commissioner is authorized to charge any deficiency to Deposit Account No. 13-2490. If Examiner Seharaseyon

believes it to be helpful, the Examiner is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: November 6, 2003

By: _____
Donald L. Zuhn, Ph.D.
Reg. No. 48,710